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Technical Note & Surgical Technique

Supratentorial neurenteric cyst: Analysis of 45 cases in the literature

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ABSTRACT

Object: Supratentorial neurenteric cysts (S-NC) are extremely rare. Patients with these lesions may present with headache, seizures or neurological deficit related to their location. Complete surgical excision, including its capsule, must be the aim of the surgery. However, strong adhesion of the cyst wall to the surrounding neurovascular structures may sometimes necessitate subtotal removal of the cyst capsule. In this study, the authors report two cases and review the literature for reported cases of S-NC to analyze clinical and radiographic presentations as well as surgical approaches and neurological outcomes.

Methods: A MEDLINE/PubMed in English language search was performed, revealing 43 S-NC cases. The authors report two additional cases in the study, resulting a total of 45 cases. Each case was analyzed for clinical presentation, lesion location, radiographic features, treatment method, and outcome.

Results: There were 25 male, 18 female and 2 newborns. The average age was 42,2 (range 0–78 years). The majority of cases (63,6%) occurred in patients between the ages of 20 and 50, but 15.9% were over 70. Frontal lobe was affected in 29 cases (64,4%), parietal lobe in 12, temporal lobe in 4, occipital in 1, and sellar or parasellar region in 4. Three cases were intraventricular. Lesions were in left side in 23 cases, in right side in 16, and on midline in 7. The majority of cases (73,3%) were extra-axial. The most common presenting symptom was headache (42,2%). The average size was 5.38 cm (greater measure) Seizures occurred in 35,5% and motor deficit in 17,7%. Other presentations were visual deficit (13,3%) and behavior changes (8,8%). Hemorrhage occurred in 2 cases, one spontaneous and one after cyst aspiration. Craniotomy with resection of the cyst (partial or complete) was performed in 95,5%. One case was treated with cyst aspiration and one case was just observed (surgery was performed in another cyst in posterior fossa). Thirty-two cases showed total improvement of symptoms, and 4 partial improvement after treatment. Two cases presented malignant transformation and two presented recurrent lesion. Complications after treatment occurred in 5 cases: 2 presented seizures in immediate postoperative period, one presented hemorrhage, one had transient SIADH. Infection occurred in just one case.

Conclusions: S-NC are rare and challenging lesions. The radiological features are nonspecific, and it is difficult to differentiate enterogenous cysts from other cystic lesions such as arachnoid cyst, epidermoid or glioependymal cyst. In cases with mass effect and refractory symptoms, surgical removal is indicated, including liquid drainage, capsule removal and cisternal communication. Resection of these lesions is associated with favorable outcomes.

1. Introduction

Neurenteric cysts (NC) are rare congenital non-neoplastic lesions that may affect the central nervous system. They are most commonly located in the spine along the ventral aspect of the spinal cord. These cysts are believed to arise from an abnormality during the brief existence of the primitive neuroenteric canal in the embryonic life that leads to an ectopic inclusion of endodermal cells into the notochord [1,2,3]. Intracranial NC are uncommon and are mainly located near the midline of the posterior fossa [1,4]. Supratentorial ocurrences have also been reported, but this location is rare and their pathogenesis is unclear [6,8,9,25].

In this manuscript, a systematic review of the literature was performed to analyze the clinical, radiological and treatment aspects of supratentorial NC (S-NC). It also reports 2 new cases of S-NC succesfully managed by cyst fenestration.

Abbreviations: NC, neurenteric cyst; S-NC, (supratentorial neurenteric cyst)

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Table 1
45 cases of S-NC reported in the literature.

	Authors & year	Age (yrs), gender	Clinical presentation	Lesion location	SIDE	Intra/ extra-axial	Size – diameter (cm)	Treatment	Outcome
1	Walls et al, 1986 [37]	40, F	Ataxia	Multiple lesions (bifrontal, posterior fossa)	Both	Intra-axial	–	Just of posterior fossa	Improved
2	Scaravilli et al, 1992 [36]	36, M	Visual loss	Optic nerve	Left	Intra-axial	–	Surgery	Unchanged
3	Leventer et al, 1994 [46]	23, F	Visual loss, opthalmoplegia	Orbit apex/superior orbital fissure	Left	Extra-axial	–	Surgery	Permanent deficit, recurrence
4	Bavetta et al, 1996 [35]	28, M	Seizures	Frontal	Right	Extra-axial	–	Surgery	Improved
5	Büttner et al, 1997 [31]	28, M	Visual loss, hydrocephalus	Third ventricle	Midline	Extra-axial	1,2	Surgery	Improved
6	Ho et al, 1998 [41]	45, F	Seizures, paresthesia	Parietal	Right	Extra-axial	–	Surgery	Partial improved. Well-differentiated papillary adenocarcinoma associated
7	Sampath et at, 1999 [28]	27, M	Headache, vomiting, ptosis	Parasselar	Left	Intra-axial	–	Surgery	Partial improved
8	Mishra et al, 2000 [30]	F	Headache, hydrocephalus	Septum pellucidum	Midline	Extra-axial	–	Surgery	Septic ventriculitis, improved
9	Cheng et al, 2002 [42]	49, M	Memory dificulties	Frontal	Right	Extra-axial	–	Surgery	Improved
10	Christov et al, 2004 [9]	31, F	Motor deficit, headache	Frontoparietal	Right	Extra-axial	–	Surgery	Improved
11	Kachur et al, 2004 [23]	35, F	Headache, seizures	Frontal	Right	Intra-axial	4	Surgery	Improved
12	Tan et al, 2004 [43]	68, F	Seizures, motor déficit	Frontal	Left	Extra-axial	6,5	Surgery	Improved
13	Preece et al, 2006 [8]	72, F	Behavior changes leading to psychosis	Frontal	Left	Extra-axial	8	Surgery	–
14	Preece el al, 2006 [8]	34, M	Seizures	Frontal	Left	Extra-axial	9	Surgery	–
15	Preece et al, 2006 [8]	78, F	Seizures	Frontal	Right	Extra-axial	7	Surgery	–
16	Preece et al, 2006 [8]	48, M	Tremor, numbness	Frontal, intra-paraventricular	Left	Extra-axial	8	Surgery	–
17	Preece et al, 2006 [8]	78, M;	Seizures	Frontal	Left	Extra-axial	7	Surgery	–
18	Neckrysh el al, 2006 [29]	70, M	Gait disturbance	Sellar	Midline	Extra-axial	4	Surgery	Transient SIADH, Improved
19	Stubenvoll el al, 2006 [44]	25, M	Seizures	Frontal	Right	Extra-axial	5,5	Surgery	Improved
20	Miyagi et al, 2007 [45]	63, M	Headache, dizziness	Parietal	Right	Extra-axial	5	Surgery	Improved
21	Takumi et al, 2008 [34]	32, M	Seizures	Frontal	Left	Extra-axial	2	Surgery	Improved
22	Marchionni et al, 2008 [47]	20, F	Headache, visual loss and motor deficit	Multiple: temporal, periisular, posterior fossa	Left	Intra-axial	–	Surgery	Partial improved
23	Mittal et al, 2009 [22]	76, F	Seizures, motor déficit	Frontoparietal	Right	Extra-axial	–	Surgery	Improved
24	Dunham et al, 2009 [40]	58, F	Headache, memory dificulties	Parietal	Right	Intra-axial	–	Surgery	Malignant transformation
25	Basheer et al, 2010 [25]	54, M	Headache	Parietooccipital	Right	Extra-axial	–	Surgery	Improved
26	Krishnamurthy et al, 2010 [48]	32, M	Motor déficit, Headache	Frontoparietal	Right	Extra-axial	8	Surgery	Seizures in the immediate postoperative period, improved
27	Krishnamurthy et al, 2010 [48]	44, F	Headache, vomiting	Frontoparietal	Left	Extra-axial	5	Surgery	Improved
28	Reddy et al, 2010 [49]	20, M	Headache, visual loss	Posterior fossa with extension into the temporal region across the tentorium	Left	Extra-axial	8	Surgery	Partial improved
29	Jhawar et al, 2011 [38]	41, M	Headache, seizures	Temporal	Right	Intra-axial	–	Surgery	Improved
30	Little et al, 2011 [32]	70, M	Gait disturbance	Sellar	Midline	Extra-axial	–	Surgery	Improved
31	Natrella et al, 2012 [18]	45, M	Seizures	Frontal	Left	Extra-axial	3,7	Surgery	Improved
32	Pulido-Rivas et al, 2012 [50]	Newborn	Increased cephalometric perimeter	Parietal	Midline	Intra-axial	4	Surgery	Improved
33	Pulido-Rivas et al, 2012 [50]	Newborn	Increased cephalometric perimeter	Frontoparietal	Right	Extra-axial	6,5	Surgery	Improved
34	Kitamura et al, 2013 [51]	28, M	Headache, loss of conscience	Frontal	Left	Intra-axial	–	Cyst aspiration	Spontaneous repetitive intracystic hemorrhage
35	Arabi et al, 2013 [52]	67, M	Seizures	Frontal	Left	Extra-axial	4,8	Surgery	Improved
36	Salvetti et al, 2013 [56]	28, F	Headache, Memory loss	Third ventricle	Midline	Extra-axial	1,1	Surgery	Improved
37	Junaid et al, 2013 [53]	35, M	Motor déficit, headache, behavior changes, seizures	Frontotemporoparietal	Right	Intra-axial	–	Surgery	Improved
38	Janczar et al, 2014 [54]	33, F	Seizures	Frontal	Left	Intra-axial	3,5	Surgery	Improved

(*continued on next page*)

Table 1 (*continued*)

	Authors & year	Age (yrs), gender	Clinical presentation	Lesion location	SIDE	Intra/ extra-axial	Size – diameter (cm)	Treatment	Outcome
39	Chakraborty et al, 2015 [55]	71, M	Hypertelorism, visual loss	Frontal, frontal and ethmoidal sinuses	Left	Extra-axial	6,4	Surgery	Improved
40	Chakraborty et al, 2015 [55]	68, F	Motor déficit, headache, behavior changes, hemorrhagic cystic mass	Frontal	Left	Extra-axial	5,5	Surgery	Improved
41	Chakraborty et al, 2015 [55]	39, F	Incidental	Frontal	Left	Intra-axial	2,3	Surgery	Unchanged
42	Rangarajan et al, 2016 [57]	52, F	Headache, Motor déficit	Frontal	Left	Extra-axial	–	Surgery	Improved
43	Rangarajan et al, 2016 [57]	32, M	Seizures	Frontal	Midline	Extra-axial	–	Surgery	Improved
44	Present case 1, 2017	46, M	Headache	Frontoparietal	Left	Extra-axial	9	Surgurgeery	Seizures in the immediate postoperative period. Improved
45	Present case 2, 2017	49, M	Headache, behavior changes	Frontal	Left	Extra-axial	5	Surgery	Improved, recurrence

2. Methods

This manuscript is a systematic review of the literature on S-NC applying the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. It also reports 2 new cases of S-NC managed by cyst fenestration. A MEDLINE/PubMed systematic article search using the key words “neurenteric cyst”, “enterogenous cyst”, “enteric cyst”, “endodermal cyst”, “gastroenterogenous cyst”, “endodermal cyst”, “archenteric cyst”, “gastrocytoma”, “supratentorial” and “intracranial” in different combinations was performed. Titles and abstracts pertaining to intracranial NC were reviewed. Moreover, reference lists of the selected articles were manually searched to identify additional studies. This method of cross-checking was continued until no additional studies were found. Then, a full-text review was independently performed by two coauthors to determine the final group of included studies. Studies were included in this review if they reported cases of S-NC. Duplicated cases were excluded. Reports written in any language other than English were also excluded.

After a final list of articles was assembled, individual patient data were extracted and inserted into a database using Microsoft Excel 2010 (Microsoft Corporation). These included patient age, gender, clinical presentation, lesion location, radiographic features, surgical treatment, and neurological outcome. Data are presented as n [5] for categorical variables and mean ± SD (median) for continuous variables. Because all studies included were small retrospective series and case reports, quantitative analysis in this review was not possible. An assessment of risk of bias was also not possible for this review. Analyses were perfromed with SAS v9.3 (SAS Institute, Cary, NC). A p value < 0.05 was considered statistically significant.

3. Results

The initial systematic MEDLINE/Pubmed search identified 30 articles. Following title and abstract review, and manual search of the reference lists of the selected articles applying the previously described inclusion and exclusion criteria, 34 studies, including 43 patients, were selected. Two other patients are reported in this article.

Among the 45 cases of S-NC were 25 male, 18 female and 2 newborns. The average age was 42,2 (range 0–78 years). The majority of cases (63,6%) occurred in patients between ages of 20 and 50, but 15.9% were over 70.

Frontal lobe was affected in 29 cases (64,4%), parietal lobe in 12, temporal lobe in 4, occipital in 1, and sellar or parasellar region in 4. Three cases were intraventricular. Lesions were in left side in 23 cases, in right side in 16, and on midline in 7. The majority of cases (73,3%) were extra-axial. The average size was 5.38 cm (greater measure).

The most common presenting symptom was headache (42,2%). Seizures occurred in 35,5% and motor deficit in 17,7%. Other symptom presentarions were visual deficit (13,3%) and behavior changes (8,8%). Hemorrhage occurred in 2 cases, one spontaneous and one after cyst aspiration.

Craniotomy with ressection of the cyst (partial or complete) was performed in 95,5%. One case was treated with cyst aspiration and one case was just observed (surgery was performed in another cyst in posterior fossa).

Thirty-two cases showed total improvement of symptoms, and 4 partial improvement after treatment. Two cases presented malignant transformation and two presented recurrent lesion. Complications after treatment occured in 5 cases: 2 presented seizures in immediate postoperative period, one presented hemorrhage, one had transient SIADH. Infection occurred in just one case. Table 1 summarizes these surgical reports/series.

4. Case report 1

A 46-year-old man presented with worsening headaches in the last

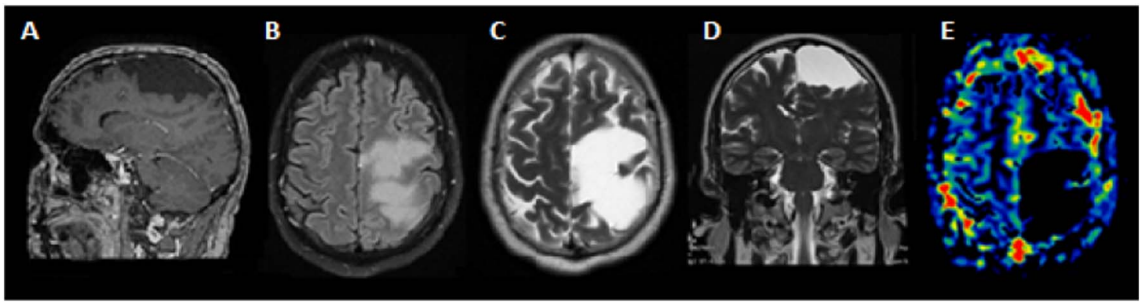

Fig. 1. Preoperative sagittal T1-weighted (A), axial Flair (B), axial T2 (C), and coronal T2 (D) MR images demonstrating an extra-axial frontoparietal cyst with intensity similar with the cerebrospinal fluid (CSF). E: Perfusion technique showing a cold region in the cyst área.

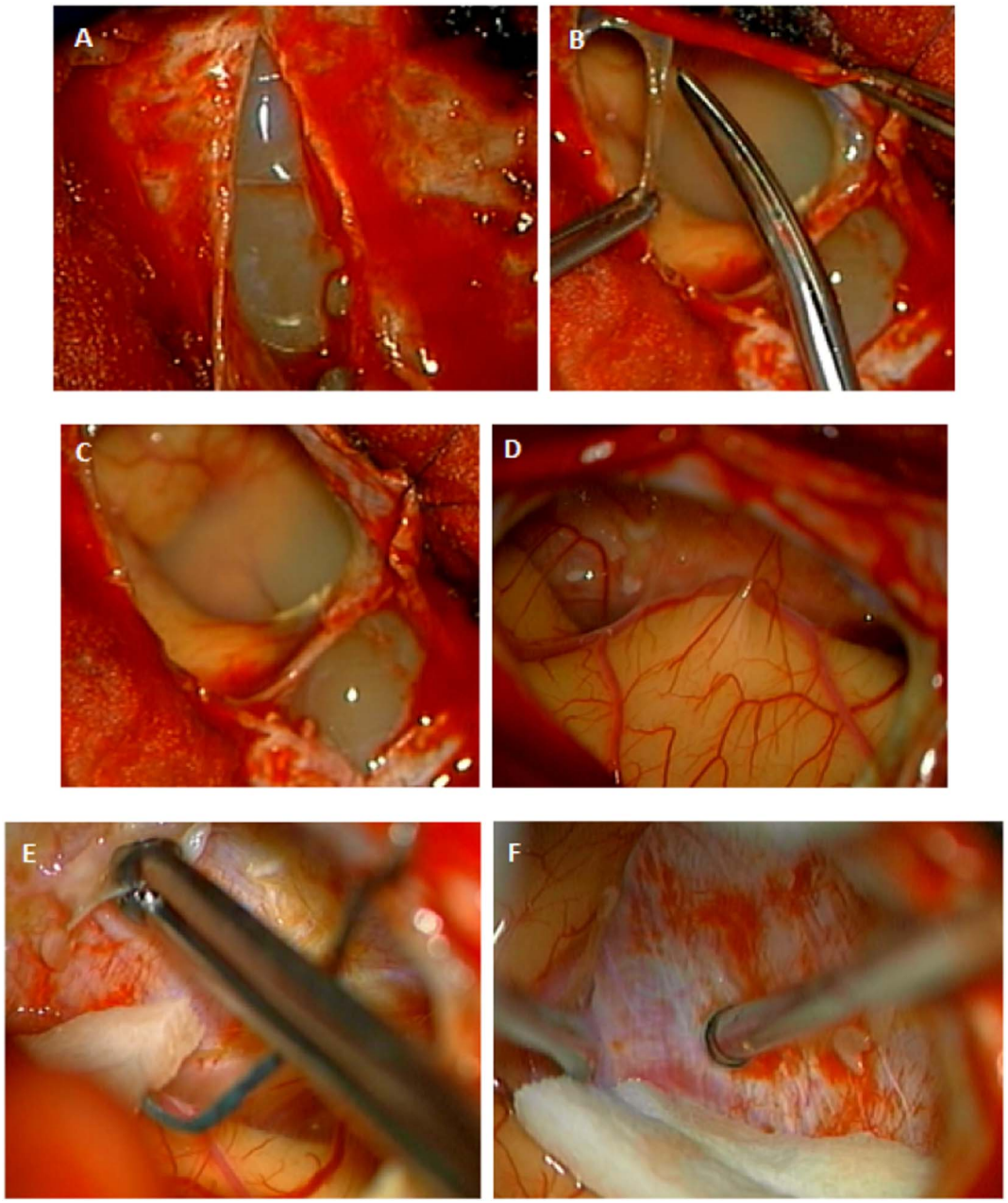

Fig. 2. A: Opening of the dura mater. Whitish capsule was viewed. B: Removal of the capsule. Presence of dense whitish content. C: Dense whitish liquid inside the cyst. D: Adhesions of the capsule to neurovascular structures. E: Removal of the capsule attached to the falx cerebri. F: Free falx cerebri and communication with the inter-hemispheric cistern.

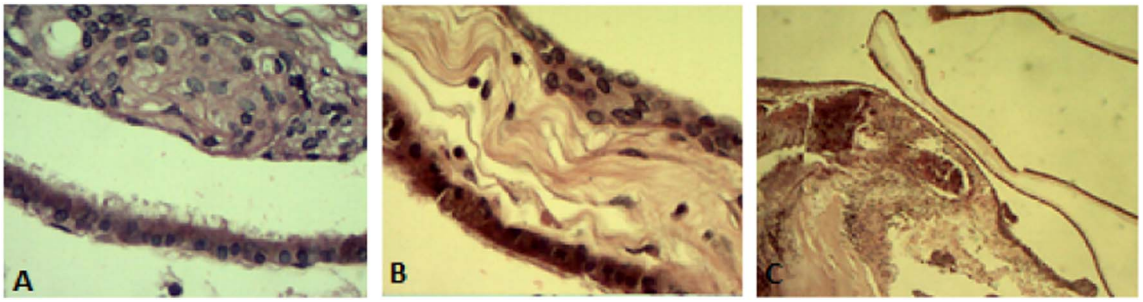

Fig. 3. Ciliated cylindrical cells supported on loose connective tissue, with groups of irregularly distributed meningothelial cells.

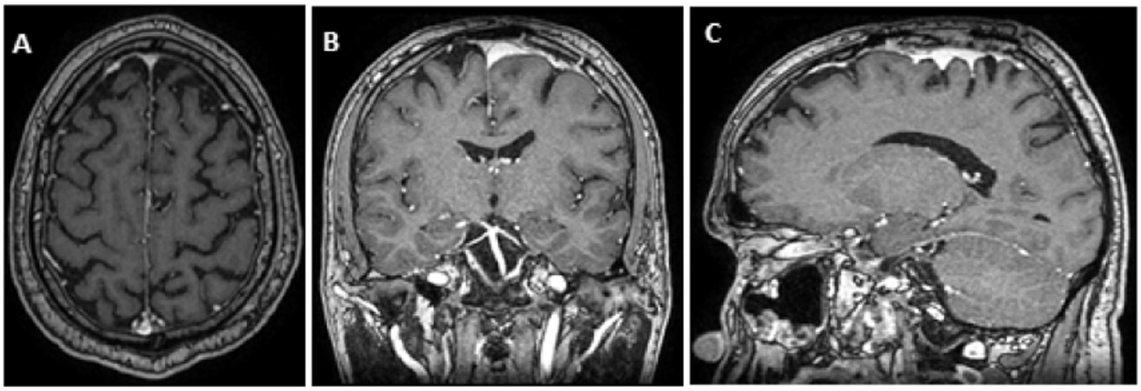

Fig. 4. Postoperative MRI in axial T1 (A), coronal (B) and sagittal (C) presenting resolution of hypertensive cyst and reexpansion of cerebral cortex.

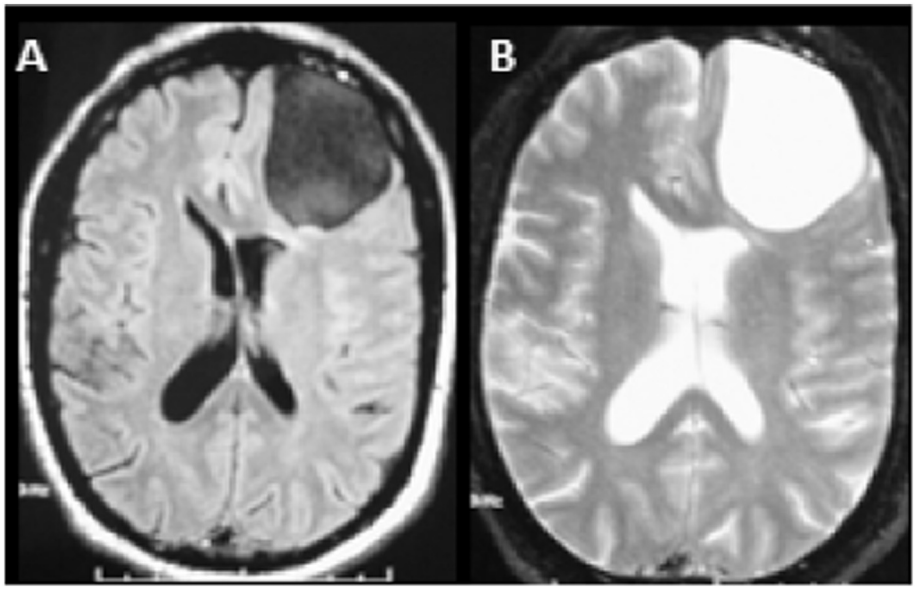

Fig. 5. Extra-axial left frontal cystic lesion, isointense to the CSF in Flair (A) and T2 (B).

month. He also complained of episodes of right-sided motor incoordination. He was known for having an intracranial cyst, which had been conservatively followed over the past 13 years. He was neurologically intact. A current brain MRI revealed a left extra-axial frontoparietal cystic lesion (9 × 5 × 5 cm) (Fig. 1), with growth over previous exams.

A left parasagittal parietal craniotomy was performed. Under microscopic visualization (Fig. 2), an encapsulated cystic lesion was drained and its capsule fenestrated with the interhemispheric subarachnoid cistern. The immediate postoperative course was complicated by recurrent seizures, which were controlled using antiepileptic drug. Otherwise, the patient completely recovered from his preoperative symptoms.

Histopathological examination showed cystic formation lined by ciliated cylindrical cells supported on loose connective tissue, with groups of irregularly distributed meningothelial cells (Fig. 3). Immunohistochemical evaluation was negative for CEA and GFAP, and positive for EMA; Ki67 was positive in < 1%. These findings were compatible with NC.

At follow-up of one year, he presented improvement of headache, without any intercurrence.

5. Case report 2

A 49-year-old man presented with behavior changes and worsening headaches for one year. A brain MRI was performed showed an extra-

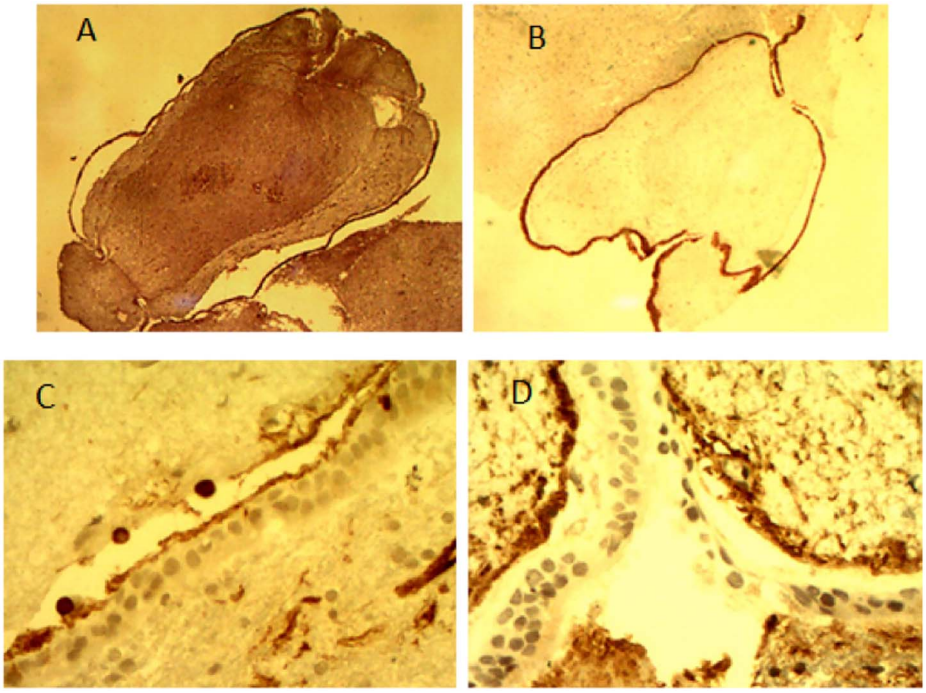

Fig. 6. A: hematoxynin-eosin analysis (10 ×) showing globular cells with regular nuclei, without glial or atypical cells, and ciliated cylindrical cells supported on loose connective tissue; B: positivity for pan-ceratin (A1–A3); C: vimentin-positive in cytoplasmic membrane; D: GFAP-negative.

axial left frontal cystic lesion. A left minifrontal craniotomy for cyst drainage and subtotal excision was performed. The postoperative course was unremarkable and the patient evolved with resolution of his preoperative symptoms (Fig. 4).

Upon 8 years of follow up, the patient presented with signs of radiological regrowth. (Fig. 5). He was neurologically intact. We performed microsurgery through previous frontal craniotomy. The contents of the cyst were drained and the cyst wall was carefully dissected, communicating widely to the cistern spaces. The patient remains asymptomatic.

Histopathology showed a liquid with globular cells with regular nuclei, without glial or atypical cells, and ciliated cylindrical cells supported on loose connective tissue. Immunohistochemical evaluation was negative for CD45, GFAP, p53, and s100 protein, and positive for A1-A3 (epithelial coating) and vimentina (Fig. 6). Ki67 was positive in < 1%.

6. Discussion

NC are endothelium-lined structures thought to be derived from malformations involving embryonal rests of primitive endodermal cells during early (third week) embryonic life [8,22]. They were first described as intestinome by Puusepp in 1934 [5]. Since then they have been called enterogenous cyst, enteric cyst, endodermal cyst, gastroenterogenous cyst, endodermal cyst, archenteric cyst and gastrocytoma [6].

NCs arise when epithelium from the gastrointestinal tract develops in an abnormal location [7,10,11]. Several theories have been proposed to explain the pathogenesis of NCs. One includes failure of separation between the notochord and the foregut leading to incorporation of primitive endodermal cells in the notochord. However, as the most rostral extent of the endoderm terminates at the level of the clivus, this hypothesis does not explain the occurrence of S-NC [23]. The “Seessel's pouch origin” hypothesis suggests a common origin for suprasellar NC, Rathke's cleft cysts and colloid cysts, This theory fails to explain laterally positioned S-NC. A third hypothesis postulates that anomalous endodermal cell migration through the primitive neurenteric canal into the ectoderm occurs dorsally, reaching far cranial and lateral positions [22].

NCs typically are encountered in the lower cervical and upper thoracic spinal levels [1,2,3,17]. Intracranial NCs are rare. Most cysts locate in the posterior fossa or craniocervical junction [7]. They have also been described in the fourth ventricle [27]. S-NC are far more uncommon that posterior fossa cysts [6,8,9,25]. They are usually larger than their infratentorial counterparts and have been described in the supra or parasellar regions [28,29], septum pellucidum [30], third ventricle [31], anterior fossa [29,32,33,34,35] and along the optic nerve [36]. There are only few reports of intraparenchymal NCs [23,37] [38],.

Clinical symptoms tend to fluctuate as a result of cyst enlargement due to active secretion of mucus by the goblets cells followed by spontaneous cyst rupture into the subarachnoidal space [24]. Headache (42,2%), seizures (35,5%), motor deficit (17,7%), visual impairment (13,3%) and behavior changes (8,8%) are the most commonly reported.

Radiologically, NCs signal intensity on MRI scans varies according to the protein content of the cysts. The majority of NCs is proteinaceous and exhibit isoto-high signal intensity on T1-weighted sequences compared with CSF. On T2-weighted sequences, most cysts show high intensity signal, whereas only few may display a hypointensity. NCs can be hyperintense on FLAIR sequences and may show partial restriction on diffusion sequences. Although uncommonly observed, Preece et al. reported mild posterior rim enhancement in their series of 18 cysts. In addition, they were not able to correlate the presence of contrast enhancement with chronic inflammatory changes due to repeated cyst rupture [8].

Differential diagnosis of NCs includes epidermoid cysts, dermoid cysts, arachnoid cysts, Rathke's cleft cysts, colloid cysts, and craniopharyngiomas. Epidermoid and dermoid cysts display moderate to intense diffusion restriction. Arachnoid cysts have the same signal intensity as CSF on all MRI sequences. Rathke and colloid cysts have a different location than NCs. Craniopharyngiomas are hyperintense on T2-weighted MR images strongly enhancing in T1 sequence with contrast agent injection.

Complete surgical excision, including cyst contents and the entirity of its capsule, is the treatment of choice. However, strong cyst adhesions to the surrounding neurovascular structures may constitute a limitation for total removal. Upon surgery, care must be taken to minimize the spill of cyst contents within the subarachnoid space,

which can lead to postoperative seizures. Perioperative administration of steroids and prophylactic antiepileptic drugs may be considered to minimize such risk. Careful radiological follow up should be performed given the risk of recurrence [7,18].

Histopathologically, NCs are benign lesions characterized by a true cyst with pseudostratified, stratified cuboidal, or columnar epithelial lining, presenting as a basement membrane. The histopathology of NC varies and can be divided into three categories: types A, B and C [21]. Type A cysts resemble respiratory or gastrointestinal epithelium and are covered by a single or pseudostratified layer of ciliated or non-ciliated cuboidal or columnar epithelium on a basement of membrane overlying fibroconnective tissue; Type B cysts are richer in connective tissue and can include smooth muscle, glandular and lymphoid tissues, and rarely nerve ganglia; Type C cysts resemble type B with the addition of glial elements. NCs are usually positive for cytokeratin, EMA, CEA, CA 19-9, negative GFAP [26] in imunohistochemistry panels.

Coexistence of S-NC and intraparenchymal subependymoma has been described [18]. Mucinous low-grade adenocarcinoma was reported to arise from an infratentorial NCs [39]. Furthermore, malignant transformation was seen in S-NC into invasive mucinous papillary cystadenocarcinoma [40] and well-differentiated papillary adenocarcinoma [41].

7. Conclusion

S-NC cysts are rare lesions. Their radiological features are nonspecific, and differential diagnosis include other cystic lesions such as arachnoid cyst, epidermoid or glioependymal cyst. Surgical treatment is recommended for symptomatic patients and includes cyst drainage, removal or fenestration with cisternal communication. Resection of these lesions is associated with favorable outcomes.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.inat.2017.08.008.

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